R.W. JOHNSON PHARM. RES. INST. USA

Individual Safety Report

3240514-3-00-01

For use by user-facilities, tributors and manufacturers for MANDATORY reporting

Page 1 of 2

Approved by FDA

Mfr report # PRIUSA1999000392

A. Patient information

1. Patient identifier: ?-? In confidence
2. Age at time of event: 26 yr or Date of birth: 03/18/1968
3. Sex: [x] female [ ] male
4. Weight: 52 lbs or ____ kgs

B. Adverse event or product problem

1. [x] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [ ] death ____
- [ ] life-threatening
- [x] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other: ____

3. Date of event: 12/13/94
4. Date of this report: 04/13/99

5. Describe event or problem

Notification via litigation of case summaries provided by physician/co-author of literature report (N Engl J Med 1997; 337:1112-7). Information provided based on extracted data from medical records of patients hospitalization for acetaminophen ingestion between 01-Jan-92 and 30-Apr-95. According to extracted data, a 26-year-old female with history of regular alcohol use took 15 tablets 325 mg acetaminophen daily for 3 weeks (not more than 4 g/24 hours) for a toothache.

Detailed information received 29-Mar-99: Medical records indicate the patient took acetaminophen in addition to acetaminopen with codeine #3 (dose, therapy dates unspecified) for wisdom tooth pain and had been self-medicating with approximately 10-15 325 mg tablets acetaminophen daily for 3 weeks. Subacute ingestion of large doses of acetaminophen (4.8 g = 80 mg/kd/day x several weeks). Last acetaminophen ingestion was approximately 8 days prior to admission (PTA). Three days PTA the patient experienced generalized fatigue, imbalance, nausea, vomiting, anorexia and dark urine.

(Cont.)

6. Relevant tests/laboratory data, including dates

16-Dec-94 urine HCG (-), ETOH (-), HBSAG (+), A-HAV (-), A-HIV1 (-), APAP level less than 1, echogram abdominal impression: liver normal in size but demonstrates prominence and increase in echogenicity of the peripheral portal branches
(Lab data cont.)

(Cont.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

No Pat Profiles Rptd
status post tubal ligation, no history liver disease, occasional alcohol use (last intake 12 days PTA, less than 2 mixed drinks)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 TYLENOL W/CODEINE NO. 3(tablet)(ACETAMINOPHEN/CODEINE)
#2 TYLENOL(PARACETAMOL)

2. Dose, frequency & route used
#1 oral
#2 325 mg, 10 in 1 day(s), oral

3. Therapy dates (if unknown, give duration)
#1 ??/???/?? - Stopped
#2 11/??/94 - 12/08/94

4. Diagnosis for use (indication)
#1 PAIN
#2 TOOTHACHE

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [x] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [x] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
No Concomitant Products Used

G. All manufacturers

1. Contact office - name/address (& mfrng site for devices)
R.W. JOHNSON PHARM. RES. INST.
USA
DIV. OF ORTHO PHARMACEUTICAL CORP.
920 U.S. Route 202
P.O. Box 300
Raritan NJ 08869
USA
(Informing Unit)

2. Phone number: 908-704-4504

3. Report source (check all that apply)
- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [x] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other: ____

4. Date received by manufacturer: 03/29/99

5. (A)NDA # 85-055
IND # ____
PLA # ____
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day [x] 15-day
- [ ] 10-day [ ] periodic
- [x] Initial [ ] follow-up # ____

8. Adverse event term(s)
1) ANOREXIA
2) URINE ABNORMAL
3) HEPATITIS
4) FATIGUE
5) DIZZINESS
6) NAUSEA
7) VOMITING

(Cont.)

9. Mfr. report number
PRIUSA1999000392

E. Initial reporter

1. Name, address & phone #
Dr. William Lee
Univ. of Texas Southwestern Medical Ctr.
5323 Harry Hines Boulevard
Dallas, TX 75235-8887
USA

2. Health professional? [x] yes [ ] no

3. Occupation: Physician

4. Initial reporter also sent report to FDA [ ] yes [ ] no [x] unk

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, or manufacturer or product caused or contributed to the event.

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3500A Facsimile

R.W. JOHNSON PHARM. RES. INST. USA
DIV. OF ORTHO PHARMACEUTICAL CORP.
920 U.S. Route 202
P.O. Box 300
Raritan NJ 08869
USA

Individual Safety Report

3240514-3-00-02

Mfr. report # : PRIUSA1999000392

Date of this report : 04/13/99

B.5 Describe event or problem (Cont...)

Two days PTA the patient developed right upper quadrant tenderness and drowsiness. The patient was admitted to the hospital on 16-Dec-94. She received full course N-acetylcysteine. Patient's hepatitis B surface antigen (+). Patient improved, liver function tests decreased and patient normalized. Patient was discharged on 19-Dec-94. Principle diagnosis was hepatitis. Other morbid conditions/complications included acetaminophen toxicity and hepatitis B infection.

Note: This is a duplicate report of a case from McNeil Consumer Healthcare reference #0905685A.

B.6 Relevant tests/laboratory data, including dates (Cont...)

Lab Result :

Sl.No.	Test date	Test name	Test result	Normal value
1	12/16/94	ALANINE AMINOTRANSFERASE	2672	
		ALBUMIN	3.6	
		ALBUMIN/GLOBULIN RATIO	1.0	
		ALKALINE PHOSPHATASE	266	
		AMYLASE	159	
		ASPARTATE AMINOTRANSFERASE	2978	
		BILIRUBIN, TOTAL	5.5	
		CARBON DIOXIDE	28	
		CHLORIDE	102	
		CREATININE	0.6	
		GLOBULIN	3.7	
		GLUCOSE	72	
		HAEMATOCRIT	35.4	
		HAEMOGLOBIN	11.7	
		PARTIAL THROMBOPLASTIN TIME	38.1	
		POTASSIUM	4.4	
		PROTHROM TIME	13.6	
		SODIUM	138	
		UREA	7	
2	12/19/94	ALANINE AMINOTRANSFERASE	1491	
		ALBUMIN	3.1	
		ALKALINE PHOSPHATASE	178	
		ASPARTATE AMINOTRANSFERASE	1055	
		BILIRUBIN, TOTAL	3.1	
		PARTIAL THROMBOPLASTIN TIME	40.6	
		PROTHROM TIME	12.8	

G. All manufacturers

8. Adverse event term(s)

8) ABDOMINAL PAIN
9) SOMNOLENCE